Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTASXS1656

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 02	STN pricing information for 2008 now available
NEWS	3	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	5	JAN 28	MARPAT searching enhanced
NEWS	6	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS	9	FEB 08	STN Express, Version 8.3, now available
NEWS	10	FEB 20	PCI now available as a replacement to DPCI
NEWS	11	FEB 25	IFIREF reloaded with enhancements
NEWS	12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS	13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS	14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS	15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS	16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS	17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS	18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	22	APR 28	IMSRESEARCH reloaded with enhancements

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 20:15:02 ON 15 MAY 2008

=> File Medline EMBASE Biosis Caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 20:15:10 ON 15 MAY 2008

FILE 'EMBASE' ENTERED AT 20:15:10 ON 15 MAY 2008

FILE 'BIOSIS' ENTERED AT 20:15:10 ON 15 MAY 2008

FILE 'CAPLUS' ENTERED AT 20:15:10 ON 15 MAY 2008

=> s (Mo25) (P) (mouse)
L1 36 (MO25) (P) (MOUSE)

=> duplicate
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
ENTER L# LIST OR (END):l1
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L1
L2 16 DUPLICATE REMOVE L1 (20 DUPLICATES REMOVED)

=> d l2 1-16 bib ab

L2 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:354110 CAPLUS
DN 148:370238
TI Insulin-resistant muscle is exercise resistant: evidence for reduced response of nuclear-encoded mitochondrial genes to exercise
AU De Filippis, Elena; Alvarez, Guy; Berria, Rachele; Cusi, Kenneth; Everman, Sarah; Meyer, Christian; Mandarino, Lawrence J.
CS Center for Metabolic Biology, Arizona State University, Tempe, AZ, USA
SO American Journal of Physiology (2008), 294(3, Pt. 1), E607-E614
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB Mitochondrial dysfunction, associated with insulin resistance, is characterized by low expression of peroxisome proliferator-activated receptor-γ coactivator-1α (PGC-1α) and nuclear-encoded mitochondrial genes. This deficit could be due to decreased phys. activity or a decreased response of gene expression to exercise. The objective of this study was to investigate whether a bout of exercise induces the same increase in nuclear-encoded mitochondrial gene expression in insulin-sensitive and insulin-resistant subjects matched for exercise capacity. Seven lean and nine obese subjects took part. Insulin sensitivity was assessed by an 80 mU·m-2·min-1 euglycemic clamp. Subjects were matched for aerobic capacity and underwent a single

bout of exercise at 70 and 90% of maximum heart rate with muscle biopsies at 30 and 300 min postexercise. Quant. RT-PCR and immunoblot analyses were used to determine the effect of exercise on gene expression and protein abundance and phosphorylation. In the postexercise period, lean subjects immediately increased PGC-1α mRNA level (reaching an eightfold increase by 300 min postexercise) and protein abundance and AMP-dependent protein kinase phosphorylation. Activation of PGC-1α was followed by increase of nuclear respiratory factor-1 and cytochrome c oxidase (subunit VIc). However, in insulin-resistant subjects, there was a delayed and reduced response in PGC-1α mRNA and protein, and phosphorylation of AMP-dependent protein kinase was transient. None of the genes downstream of PGC-1α was increased after exercise in insulin resistance. Insulin-resistant subjects have a reduced response of nuclear-encoded mitochondrial genes to exercise, and this could contribute to the origin and maintenance of mitochondrial dysfunction.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 16 MEDLINE on STN DUPLICATE 1
AN 2007078449 MEDLINE
DN PubMed ID: 16985256
TI Effects of 3-phosphoglycerate and other metabolites on the activation of AMP-activated protein kinase by LKB1-STRAD-MO25.
AU Ellingson W J; Chesser D G; Winder W W
CS Department of Physiology and Developmental Biology, Brigham Young University, Provo, Utah 84602, USA.
SO American journal of physiology. Endocrinology and metabolism, (2007 Feb) Vol. 292, No. 2, pp. E400-7. Electronic Publication: 2006-09-19.
Journal code: 100901226. ISSN: 0193-1849.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200703
ED Entered STN: 7 Feb 2007
Last Updated on STN: 20 Mar 2007
Entered Medline: 19 Mar 2007
AB Skeletal muscle contraction results in the phosphorylation and activation of the AMP-activated protein kinase (AMPK) by an upstream kinase (AMPKK). The LKB1-STE-related adaptor (STRAD)-mouse protein 25 (MO25) complex is the major AMPKK in skeletal muscle; however, LKB1-STRAD-MO25 activity is not increased by muscle contraction. This relationship suggests that phosphorylation of AMPK by LKB1-STRAD-MO25 during skeletal muscle contraction may be regulated by allosteric mechanisms. In this study, we tested an array of metabolites including, glucose 6-phosphate, fructose 6-phosphate, fructose 1,6-bisphosphate, 3-phosphoglycerate (3-PG), glucose 1-phosphate, glucose 1,6-bisphosphate, ADP, carnitine, acetylcarnitine, IMP, inosine, and ammonia for allosteric regulation. ADP inhibited both AMPK and LKB1-STRAD-MO25 actions, but probably is not important physiologically because of the low free ADP inside the muscle fiber. We found that 3-PG stimulated LKB1-STRAD-MO25 activity and allowed for increased AMPK phosphorylation. 3-PG did not stimulate LKB1-STRAD-MO25 activity toward the peptide substrate LKB1tide. These results have identified 3-PG as an AMPK-specific regulator of AMPK phosphorylation and activation by LKB1-STRAD-MO25.

L2 ANSWER 3 OF 16 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
AN 2007078191 EMBASE
TI Effects of 3-phosphoglycerate and other metabolites on the activation of

AMP-activated protein kinase by LKB1-STRAD-MO25.
AU Ellingson, W.J.; Chesser, D.G.; Winder, W.W. (correspondence)
CS Department of Physiology and Developmental Biology, Brigham Young University, Provo, UT, United States. william_winder@byu.edu
AU Winder, W.W. (correspondence)
CS 545 WIDB, Brigham Young Univ., Provo, UT 84602, United States. william_winder@byu.edu
SO American Journal of Physiology - Endocrinology and Metabolism, (Feb 2007) Vol. 292, No. 2, pp. E400-E407.
Refs: 47
ISSN: 0193-1849 E-ISSN: 1522-1555 CODEN: AJPMD9
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 1 Mar 2007
Last Updated on STN: 1 Mar 2007
AB Skeletal muscle contraction results in the phosphorylation and activation of the AMP-activated protein kinase (AMPK) by an upstream kinase (AMPKK). The LKB1-STE-related adaptor (STRAD)-mouse protein 25 (MO25) complex is the major AMPKK in skeletal muscle; however, LKB1-STRAD-MO25 activity is not increased by muscle contraction. This relationship suggests that phosphorylation of AMPK by LKB1-STRAD-MO25 during skeletal muscle contraction may be regulated by allosteric mechanisms. In this study, we tested an array of metabolites including, glucose 6-phosphate, fructose 6-phosphate, fructose 1,6-bisphosphate, 3-phosphoglycerate (3-PG), glucose 1-phosphate, glucose 1,6-bisphosphate, ADP, carnitine, acetylcarnitine, IMP, inosine, and ammonia for allosteric regulation. ADP inhibited both AMPK and LKB1-STRAD-MO25 actions, but probably is not important physiologically because of the low free ADP inside the muscle fiber. We found that 3-PG stimulated LKB1-STRAD-MO25 activity and allowed for increased AMPK phosphorylation. 3-PG did not stimulate LKB1-STRAD-MO25 activity toward the peptide substrate LKB1tide. These results have identified 3-PG as an AMPK-specific regulator of AMPK phosphorylation and activation by LKB1-STRAD-MO25.

L2 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 2
AN 2006105532 MEDLINE
DN PubMed ID: 16396636
TI The ubiquitin-associated domain of AMPK-related kinases regulates conformation and LKB1-mediated phosphorylation and activation.
AU Jaleel Mahaboobi; Villa Fabrizio; Deak Maria; Toth Rachel; Prescott Alan R; Van Aalten Daan M F; Alessi Dario R
CS MRC Protein Phosphorylation Unit, MSI/WTB Complex, University of Dundee, Dow Street, Dundee DD1 5EH, Scotland, UK.. a.mahaboobi@dundee.ac.uk
SO The Biochemical journal, (2006 Mar 15) Vol. 394, No. Pt 3, pp. 545-55.
Journal code: 2984726R. E-ISSN: 1470-8728.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200607
ED Entered STN: 23 Feb 2006
Last Updated on STN: 29 Jul 2006
Entered Medline: 28 Jul 2006
AB Recent work indicates that the LKB1 tumour suppressor protein kinase, which is mutated in Peutz-Jeghers cancer syndrome, phosphorylates and

activates a group of protein kinases that are related to AMPK (AMP-activated protein kinase). Ten of the 14 AMPK-related protein kinases activated by LKB1, including SIK (salt-induced kinase), MARK (microtubule-affinity-regulating kinase) and BRSK (brain-specific kinase) isoforms, possess a ubiquitin-associated (UBA) domain immediately C-terminal to the kinase catalytic domain. These are the only protein kinases in the human genome known to possess a UBA domain, but their roles in regulating AMPK-related kinases are unknown. We have investigated the roles that the UBA domain may play in regulating these enzymes. Limited proteolysis of MARK2 revealed that the kinase and UBA domains were contained within a fragment that was resistant to trypsin proteolysis. SAXS (small-angle X-ray scattering) analysis of inactive and active LKB1-phosphorylated MARK2 revealed that activation of MARK2 is accompanied by a significant conformational change that alters the orientation of the UBA domain with respect to the catalytic domain. Our results indicate that none of the UBA domains found in AMPK-related kinases interact with polyubiquitin or other ubiquitin-like molecules. Instead, the UBA domains appear to play an essential conformational role and are required for the LKB1-mediated phosphorylation and activation of AMPK-related kinases. This is based on the findings that mutation or removal of the UBA domains of several AMPK-related kinases, including isoforms of MARK, SIK and BRSK, markedly impaired the catalytic activity and LKB1-mediated phosphorylation of these enzymes. We also provide evidence that the UBA domains do not function as LKB1-STRAD (STE20-related adaptor)-MO25 (mouse protein 25) docking/interacting sites and that mutations in the UBA domain of SIK suppressed the ability of SIK to localize within punctate regions of the nucleus. Taken together, these findings suggest that the UBA domains of AMPK-related kinases play an important role in regulating the conformation, activation and localization of these enzymes.

L2 ANSWER 5 OF 16 MEDLINE on STN DUPLICATE 3
AN 2006342946 MEDLINE
DN PubMed ID: 16756488
TI LKB1-dependent signaling pathways.
AU Alessi Dario R; Sakamoto Kei; Bayascas Jose R
CS Medical Research Council, Protein Phosphorylation Unit, School of Life Sciences, University of Dundee, Dundee DD1 5EH, Scotland.. d.r.alessi@dundee.ac.uk
SO Annual review of biochemistry, (2006) Vol. 75, pp. 137-63. Ref: 139
Journal code: 2985150R. ISSN: 0066-4154.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200702
ED Entered STN: 8 Jun 2006
Last Updated on STN: 6 Feb 2007
Entered Medline: 5 Feb 2007
AB This review focuses on remarkable recent findings concerning the mechanism by which the LKB1 protein kinase that is mutated in Peutz-Jeghers cancer syndrome operates as a tumor suppressor. We discuss evidence that the cellular localization and activity of LKB1 is controlled through its interaction with a catalytically inactive protein resembling a protein kinase, termed STRAD, and an armadillo repeat-containing protein, named mouse protein 25 (MO25). The data suggest that LKB1 functions as a tumor suppressor by not only inhibiting proliferation, but also by exerting profound effects on cell polarity and, most unexpectedly, on the ability of a cell to detect and respond to low cellular energy levels. Genetic and biochemical findings indicate that LKB1 exerts its

effects by phosphorylating and activating 14 protein kinases, all related to the AMP-activated protein kinase. The work described in this review shows how a study of an obscure cancer syndrome can uncover new and important regulatory pathways, relevant to the understanding of multiple human diseases.

L2 ANSWER 6 OF 16 MEDLINE on STN DUPLICATE 4
AN 2005600805 MEDLINE
DN PubMed ID: 16014350
TI Endurance training increases skeletal muscle LKB1 and PGC-1alpha protein abundance: effects of time and intensity.
AU Taylor Eric B; Lamb Jeremy D; Hurst Richard W; Chesser David G; Ellingson William J; Greenwood Lyle J; Porter Brian B; Herway Seth T; Winder William W
CS Department of Physiology and Developmental Biology, 545 WIDB, Brigham Young University, Provo, UT 84602, USA.
NC AR 41438 (United States NIAMS)
SO American journal of physiology. Endocrinology and metabolism, (2005 Dec) Vol. 289, No. 6, pp. E960-8. Electronic Publication: 2005-07-12. Journal code: 100901226. ISSN: 0193-1849.
CY United States
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LA English
FS Priority Journals
EM 200512
ED Entered STN: 11 Nov 2005
Last Updated on STN: 22 Dec 2005
Entered Medline: 21 Dec 2005
AB Recent research suggests that LKB1 is the major AMP-activated protein kinase kinase (AMPKK). Peroxisome-proliferator-activated receptor-gamma coactivator-1alpha (PGC-1alpha) is a master coordinator of mitochondrial biogenesis. Previously we reported that skeletal muscle LKB1 protein increases with endurance training. The purpose of this study was to determine whether training-induced increases in skeletal muscle LKB1 and PGC-1alpha protein exhibit a time course and intensity-dependent response similar to that of citrate synthase. Male Sprague-Dawley rats completed endurance- and interval-training protocols. For endurance training, rats trained for 4, 11, 25, or 53 days. Interval-training rats trained identically to endurance-trained rats, except that after 25 days interval training was combined with endurance training. Time course data were collected from endurance-trained red quadriceps (RQ) after each time point. Interval training data were collected from soleus, RQ, and white quadriceps (WQ) muscle after 53 days only. Mouse protein 25 (MO25) and PGC-1alpha protein increased significantly after 4 days. Increased citrate synthase activity, increased LKB1 protein, and decreased AMPKK activity were found after 11 days. Maximal increases occurred after 4 days for hexokinase II, 25 days for MO25, and 53 days for citrate synthase, LKB1, and PGC-1alpha. In WQ, but not RQ or soleus, interval training had an additive effect to endurance training and induced significant increases in all proteins measured. These results demonstrate that LKB1 and PGC-1alpha protein abundances increase with endurance and interval training similarly to citrate synthase. The increase in LKB1 and PGC-1alpha with endurance and interval training may function to maintain the training-induced increases in mitochondrial mass.

L2 ANSWER 7 OF 16 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
AN 2006214360 EMBASE
TI Endurance training increases skeletal muscle LKB1 and PGC-1α protein

abundance: Effects of time and intensity.
AU Taylor, Eric B.; Lamb, Jeremy D.; Hurst, Richard W.; Chesser, David G.; Ellingson, William J.; Greenwood, Lyle J.; Porter, Brian B.; Herway, Seth T.; Winder, William W. (correspondence)
CS Department of Physiology and Developmental Biology, Brigham Young University, Provo, UT, United States. william_winder@byu.edu
AU Winder, William W. (correspondence)
CS 545 WIDB, Brigham Young University, Provo, UT 84602, United States. william_winder@byu.edu
SO American Journal of Physiology - Endocrinology and Metabolism, (Dec 2005) Vol. 289, No. 6, pp. E960-E968.
Refs: 68
ISSN: 0193-1849 E-ISSN: 1522-1555 CODEN: AJPMD9
CY United States
DT Journal; Article
FS 002 Physiology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 30 May 2006
Last Updated on STN: 30 May 2006
AB Recent research suggests that LKB1 is the major AMP-activated protein kinase kinase (AMPKK). Peroxisome-proliferator-activated receptor-γ coactivator-1α (PGC-1α) is a master coordinator of mitochondrial biogenesis. Previously we reported that skeletal muscle LKB1 protein increases with endurance training. The purpose of this study was to determine whether training-induced increases in skeletal muscle LKB1 and PGC-1α protein exhibit a time course and intensity-dependent response similar to that of citrate synthase. Male Sprague-Dawley rats completed endurance- and interval-training protocols. For endurance training, rats trained for 4, 11, 25, or 53 days. Interval-training rats trained identically to endurance-trained rats, except that after 25 days interval training was combined with endurance training. Time course data were collected from endurance-trained red quadriceps (RQ) after each time point. Interval training data were collected from soleus, RQ, and white quadriceps (WQ) muscle after 53 days only. Mouse protein 25 (MO25) and PGC-1α protein increased significantly after 4 days. Increased citrate synthase activity, increased LKB1 protein, and decreased AMPKK activity were found after 11 days. Maximal increases occurred after 4 days for hexokinase II, 25 days for MO25, and 53 days for citrate synthase, LKB1, and PGC-1α. In WQ, but not RQ or soleus, interval training had an additive effect to endurance training and induced significant increases in all proteins measured. These results demonstrate that LKB1 and PGC-1α protein abundances increase with endurance and interval training similarly to citrate synthase. The increase in LKB1 and PGC-1α with endurance and interval training may function to maintain the training-induced increases in mitochondrial mass. Copyright .COPYRGT. 2005 the American Physiological Society.

L2 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:113852 CAPLUS
DN 142:174293
TI Analysis of the LKB1-STRAD-MO25 complex
AU Boudeau, Jerome; Scott, John W.; Resta, Nicoletta; Deak, Maria; Kieloch, Agnieszka; Komander, David; Hardie, D. Grahame; Prescott, Alan R.; Van Aalten, Daan M. F.; Alessi, Dario R.
CS MRC Protein Phosphorylation Unit, University of Dundee, Dundee, DD1 5EH, UK
SO Journal of Cell Science (2004), 117(26), 6365-6375
CODEN: JNCSAI; ISSN: 0021-9533

PB Company of Biologists Ltd.
DT Journal
LA English
AB Mutations in the LKB1 tumor suppressor threonine kinase cause the inherited Peutz-Jeghers cancer syndrome and are also observed in some sporadic cancers. Recent work indicates that LKB1 exerts effects on metabolism, polarity and proliferation by phosphorylating and activating protein kinases belonging to the AMPK subfamily. In vivo, LKB1 forms a complex with STRAD, an inactive pseudo-kinase, and MO25, an armadillo repeat scaffolding-like protein. Binding of LKB1 to STRAD-MO25 activates LKB1 and re-localizes it from the nucleus to the cytoplasm. To learn more about the inherent properties of the LKB1-STRAD-MO25 complex, we first investigated the activity of 34 point mutants of LKB1 found in human cancers and their ability to interact with STRAD and MO25. Interestingly, 12 of these mutants failed to interact with STRAD-MO25. Performing mutagenesis anal., we defined two binding sites located on opposite surfaces of MO25α, which are required for the assembly of MO25α into a complex with STRADα and LKB1. In addition, we demonstrate that LKB1 does not require phosphorylation of its own T-loop to be activated by STRADα-MO25α, and discuss the possibility that this unusual mechanism of regulation arises from LKB1 functioning as an upstream kinase. Finally, we establish that STRADα, despite being catalytically inactive, is still capable of binding ATP with high affinity, but that this is not required for activation of LKB1. Taken together, our findings reinforce the functional importance of the binding of LKB1 to STRAD, and provide a greater understanding of the mechanism by which LKB1 is regulated and activated through its interaction with STRAD and MO25.
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 16 MEDLINE on STN DUPLICATE 5
AN 2004048988 MEDLINE
DN PubMed ID: 14730349
TI Crystal structure of MO25 alpha in complex with the C terminus of the pseudo kinase STE20-related adaptor.
AU Milburn Christine C; Boudeau Jerome; Deak Maria; Alessi Dario R; van Aalten Daan M F
CS Division of Biological Chemistry & Molecular Microbiology, School of Life Sciences, University of Dundee, Dundee DD1 5EH, Scotland.
SO Nature structural & molecular biology, (2004 Feb) Vol. 11, No. 2, pp. 193-200. Electronic Publication: 2004-01-18.
Journal code: 101186374. ISSN: 1545-9993.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
OS PDB-1UPK; PDB-1UPL
EM 200404
ED Entered STN: 30 Jan 2004
Last Updated on STN: 6 Apr 2004
Entered Medline: 5 Apr 2004
AB Mouse protein 25 alpha (MO25 alpha) is a 40-kDa protein that, together with the STE20-related adaptor-alpha (STRAD alpha) pseudo kinase, forms a regulatory complex capable of stimulating the activity of the LKB1 tumor suppressor protein kinase. The latter is mutated in the inherited Peutz-Jeghers cancer syndrome (PJS). MO25 alpha binds directly to a conserved Trp-Glu-Phe sequence at the STRAD alpha C terminus, markedly enhancing binding of STRAD alpha to LKB1 and increasing LKB1 catalytic activity. The MO25 alpha

crystal structure reveals a helical repeat fold, distantly related to the Armadillo proteins. A complex with the STRAD alpha peptide reveals a hydrophobic pocket that is involved in a unique and specific interaction with the Trp-Glu-Phe motif, further supported by mutagenesis studies. The data represent a first step toward structural analysis of the LKB1-STRAD-MO25 complex, and suggests that MO25 alpha is a scaffold protein to which other regions of STRAD-LKB1, cellular LKB1 substrates or regulatory components could bind.

L2 ANSWER 10 OF 16 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
AN 2003486151 EMBASE
TI Complexes between the LKB1 tumor suppressor, STRADα/β and MO25α/β are upstream kinases in the AMP-activated protein kinase cascade.
AU Hawley, Simon A.; Reid, Jennifer L.; Mustard, Kirsty J.; Hardie, D. Grahame
CS Division of Molecular Physiology, Wellcome Trust Biocentre, University of Dundee, Dundee DD1 5EH, United Kingdom. d.g.hardie@dundee.ac.uk
AU Boudeau, Jerome; Alessi, Dario R. (correspondence)
CS MRC Protein Phosphorylation Unit, Wellcome Trust Biocentre, University of Dundee, Dundee DD1 5EH, United Kingdom. d.r.alessi@dundee.ac.uk
AU Udd, Lina; Makela, Tomi P.
CS Molecular Cancer Biology Program, Helsinki University Central Hospital, University of Helsinki, Helsinki, Finland.
SO Journal of Biology, (2003) Vol. 2, No. 4, pp. 281-2815.
Refs: 49
ISSN: 1475-4924 CODEN: JBOIAW
CY United Kingdom
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 30 Dec 2003
Last Updated on STN: 30 Dec 2003
AB Background: The AMP-activated protein kinase (AMPK) cascade is a sensor of cellular energy charge that acts as a 'metabolic master switch' and inhibits cell proliferation. Activation requires phosphorylation of Thr172 of AMPK within the activation loop by upstream kinases (AMPKKs) that have not been identified. Recently, we identified three related protein kinases acting upstream of the yeast homolog of AMPK. Although they do not have obvious mammalian homologs, they are related to LKB1, a tumor suppressor that is mutated in the human Peutz-Jeghers cancer syndrome. We recently showed that LKB1 exists as a complex with two accessory subunits, STRADα/β and MO25α/β. Results: We report the following observations. First, two AMPKK activities purified from rat liver contain LKB1, STRADα and MO25 α, and can be immunoprecipitated using anti-LKB1 antibodies. Second, both endogenous and recombinant complexes of LKB1, STRADα/β and MO25α/β activate AMPK via phosphorylation of Thr172. Third, catalytically active LKB1, STRADα or STRADβ and MO25α or MO25β are required for full activity. Fourth, the AMPK-activating drugs AICA riboside and phenformin do not activate AMPK in HeLa cells (which lack LKB1), but activation can be restored by stably expressing wild-type, but not catalytically inactive, LKB1. Fifth, AICA riboside and phenformin fail to activate AMPK in immortalized fibroblasts from LKB1-knockout mouse embryos. Conclusions: These results provide the first description of a physiological substrate for the LKB1 tumor suppressor and

suggest that it functions as an upstream regulator of AMPK. Our findings indicate that the tumors in Peutz-Jeghers syndrome could result from deficient activation of AMPK as a consequence of LKB1 inactivation.

L2 ANSWER 11 OF 16 MEDLINE on STN
AN 2004353523 MEDLINE
DN PubMed ID: 14511394
TI Complexes between the LKB1 tumor suppressor, STRAD alpha/beta and MO25 alpha/beta are upstream kinases in the AMP-activated protein kinase cascade.
AU Hawley Simon A; Boudeau Jerome; Reid Jennifer L; Mustard Kirsty J; Udd Lina; Makela Tomi P; Alessi Dario R; Hardie D Grahame
CS Division of Molecular Physiology, University of Dundee, Dundee DD1 5EH, UK.
SO Journal of biology, (2003) Vol. 2, No. 4, pp. 28. Electronic Publication: 2003-09-24.
Journal code: 101147570. E-ISSN: 1475-4924.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200412
ED Entered STN: 17 Jul 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 14 Dec 2004
AB BACKGROUND: The AMP-activated protein kinase (AMPK) cascade is a sensor of cellular energy charge that acts as a 'metabolic master switch' and inhibits cell proliferation. Activation requires phosphorylation of Thr172 of AMPK within the activation loop by upstream kinases (AMPKKs) that have not been identified. Recently, we identified three related protein kinases acting upstream of the yeast homolog of AMPK. Although they do not have obvious mammalian homologs, they are related to LKB1, a tumor suppressor that is mutated in the human Peutz-Jeghers cancer syndrome. We recently showed that LKB1 exists as a complex with two accessory subunits, STRAD alpha/beta and MO25 alpha/beta.
RESULTS: We report the following observations. First, two AMPKK activities purified from rat liver contain LKB1, STRAD alpha and MO25 alpha, and can be immunoprecipitated using anti-LKB1 antibodies. Second, both endogenous and recombinant complexes of LKB1, STRAD alpha/beta and MO25 alpha/beta activate AMPK via phosphorylation of Thr172. Third, catalytically active LKB1, STRAD alpha or STRAD beta and MO25 alpha or MO25 beta are required for full activity. Fourth, the AMPK-activating drugs AICA riboside and phenformin do not activate AMPK in HeLa cells (which lack LKB1), but activation can be restored by stably expressing wild-type, but not catalytically inactive, LKB1. Fifth, AICA riboside and phenformin fail to activate AMPK in immortalized fibroblasts from LKB1-knockout mouse embryos. CONCLUSIONS: These results provide the first description of a physiological substrate for the LKB1 tumor suppressor and suggest that it functions as an upstream regulator of AMPK. Our findings indicate that the tumors in Peutz-Jeghers syndrome could result from deficient activation of AMPK as a consequence of LKB1 inactivation.

L2 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:125511 CAPLUS
DN 141:136077
TI Complexes between the LKB1 tumor suppressor, STRADα/β and MO25α/β are upstream kinases in the AMP-activated protein kinase cascade
AU Hawley, Simon A.; Boudeau, Jerome; Reid, Jennifer L.; Mustard, Kirsty J.;

Udd, Lina; Makela, Tomi P.; Alessi, Dario R.; Hardie, D. Grahame
CS Wellcome Trust Biocentre, University of Dundee, Dundee, DD1 5EH, UK
SO Journal of Biology (London, United Kingdom) (2003), 2(4), No pp. given
CODEN: JBOIAW; ISSN: 1475-4924
URL: http://jbiol.com/content/pdf/1475-4924-2-28.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Background: The AMP-activated protein kinase (AMPK) cascade is a sensor of cellular energy charge that acts as a 'metabolic master switch' and inhibits cell proliferation. Activation requires phosphorylation of Thr172 of AMPK within the activation loop by upstream kinases (AMPKKs) that have not been identified. Recently, we identified three related protein kinases acting upstream of the yeast homolog of AMPK. Although they do not have obvious mammalian homologs, they are related to LKB1, a tumor suppressor that is mutated in the human Peutz-Jeghers cancer syndrome. We recently showed that LKB1 exists as a complex with two accessory subunits, STRADα/β and MO25α/β.
Results: We report the following observations. First, two AMPKK activities purified from rat liver contain LKB1, STRADα and MO25α, and can be immunopptd. using anti-LKB1 antibodies. Second, both endogenous and recombinant complexes of LKB1, STRADα and MO25β activate AMPK via phosphorylation of Thr172. Third, catalytically active LKB1, STRADα or STRADβ and MO25α or MO25β are required for full activity. Fourth, the AMPK-activating drugs AICA riboside and phenformin do not activate AMPK in HeLa cells (which lack LKB1), but activation can be restored by stably expressing wild-type, but not catalytically inactive, LKB1. Fifth, AICA riboside and phenformin fail to activate AMPK in immortalized fibroblasts from LKB1-knockout mouse embryos.
Conclusions: These results provide the first description of a physiol. substrate for the LKB1 tumor suppressor and suggest that it functions as an upstream regulator of AMPK. Our findings indicate that the tumors in Peutz-Jeghers syndrome could result from deficient activation of AMPK as a consequence of LKB1 inactivation.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 16 MEDLINE on STN DUPLICATE 6
AN 1999126010 MEDLINE
DN PubMed ID: 9928930
TI Molecular characterization of HymA, an evolutionarily highly conserved and highly expressed protein of Aspergillus nidulans.
AU Karos M; Fischer R
CS Laboratorium fur Mikrobiologie, Philipps-Universitat Marburg and Max-Planck-Institut fur terrestrische Mikrobiologie, Germany.
SO Molecular & general genetics : MGG, (1999 Jan) Vol. 260, No. 6, pp. 510-21.
Journal code: 0125036. ISSN: 0026-8925.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
OS GENBANK-AJ001157
EM 199902
ED Entered STN: 1 Mar 1999
Last Updated on STN: 4 Mar 2003
Entered Medline: 18 Feb 1999
AB Aspergillus nidulans reproduces asexually via uninucleate, haploid spores, which are produced on morphologically differentiated aerial structures,

called conidiophores. These consist of four distinct cell types, a foot with a terminally swollen stalk, metulae, phialides and conidiospores. The molecular mechanisms underlying the morphological changes that occur during conidiophore development have been studied by mutant analysis. We have isolated the hym A mutant, in which conidiophore development is affected at the metula stage. In the mutant metulae do not differentiate properly but come to resemble hyphae (hym = hypha-like metulae). In this paper we have analyzed the corresponding gene. It encodes a highly expressed 44 kDa protein which resides in the cytoplasm and has homologues in yeast, plants, fly, worm, fish, mice and man. We constructed hym deletion strains of Saccharomyces cerevisiae and of A. nidulans and found that the gene is essential in S. cerevisiae but is dispensable in the filamentous fungus. A cellular function for the Hym protein has not yet been defined in any organism. To demonstrate functional conservation we constructed a chimeric protein comprised of the N-terminal half of the A. nidulans and the C-terminal half of the mouse homologue MO25. This hybrid protein could fully substitute for HymA function in A. nidulans. In addition, the mouse protein itself partially rescued the hym A mutation in the fungus. HymA is thus highly conserved in evolution and probably serves similar functions. The fact that hym A is required for conidiophore development in A. nidulans suggests that homologous genes in other organisms might also be involved in morphogenesis.

L2 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:112463 CAPLUS
DN 130:321416
TI Molecular characterization of HymA, an evolutionarily highly conserved and highly expressed protein of Aspergillus nidulans
AU Karos, M.; Fischer, R.
CS Laboratorium fur Mikrobiologie Philipps-Universitat Marburg, Max-Planck-Institut fur terrestrische Mikrobiologie Karl-von-Frisch-Str., Marburg, D-35043, Germany
SO Molecular and General Genetics (1998), 260(6), 510-521
CODEN: MGGEAE; ISSN: 0026-8925
PB Springer-Verlag
DT Journal
LA English
AB Aspergillus nidulans reproduces asexually via uninucleate, haploid spores, which are produced on morphol. differentiated aerial structures, called conidiophores. These consist of four distinct cell types, a foot with a terminally swollen stalk, metulae, phialides and conidiospores. The mol. mechanisms underlying the morphol. changes that occur during conidiophore development have been studied by mutant anal. We have isolated the hymA mutant, in which conidiophore development is affected at the metula stage. In the mutant metulae do not differentiate properly but come to resemble hyphae (hym = hypha-like metulae). In this paper we have analyzed the corresponding gene. It encodes a highly expressed 44 kDa protein which resides in the cytoplasm and has homologues in yeast, plants, fly, worm, fish, mice and man. We constructed hym deletion strains of Saccharomyces cerevisiae and of A. nidulans and found that the gene is essential in S. cerevisiae but is dispensable in the filamentous fungus. A cellular function for the Hym protein has not yet been defined in any organism. To demonstrate functional conservation we constructed a chimeric protein comprised of the N-terminal half of the A. nidulans and the C-terminal half of the mouse homolog MO25. This hybrid protein could fully substitute for HymA function in A. nidulans. In addition, the mouse protein itself partially rescued the hymA mutation in the fungus. HymA is thus highly conserved in evolution and probably serves similar functions. The fact that hymA is required for conidiophore development in A. nidulans suggests that homologous genes in other

organisms might also be involved in morphogenesis.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 16 MEDLINE on STN DUPLICATE 7
AN 96268479 MEDLINE
DN PubMed ID: 8672247
TI Molecular characterization of the Drosophila Mo25 gene, which is conserved among Drosophila, mouse, and yeast.
AU Nozaki M; Onishi Y; Togashi S; Miyamoto H
CS Research Institute for Microbial Diseases, Osaka University, Osaka, Japan.
SO DNA and cell biology, (1996 Jun) Vol. 15, No. 6, pp. 505-9.
Journal code: 9004522. ISSN: 1044-5498.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
OS GENBANK-AB000402
EM 199608
ED Entered STN: 22 Aug 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 12 Aug 1996
AB To study the general physiological role of the Mo25 gene, which has been cloned from mouse cleavage-stage embryos, we isolated a Drosophila equivalent, dMo25, cDNA from an embryo cDNA library. The 2,222 nucleotides contained a single open reading frame encoding a polypeptide of 339 amino acid residues with a calculated molecular mass of 39,278 daltons. The deduced amino acid sequence of the dMo25 cDNA had 69.3% identity with mouse Mo25. A homology search revealed that these were similar to a protein encoded in an open reading frame near the calcineurin B subunit gene on chromosome XI in Saccharomyces cerevisiae. In particular, the carboxy-terminal region was highly conserved in Drosophila, mouse, and yeast. The dMo25 gene was mapped to the left arm of the third chromosome at 73AB, and 2.3- and 1.8-kb mRNA bands were detected during development and in adult Drosophila. Conservation of the gene structure and the wide expression profile indicated that the function of the gene is likely to be fundamental in many cell types as well as during development.

L2 ANSWER 16 OF 16 MEDLINE on STN DUPLICATE 8
AN 93119656 MEDLINE
DN PubMed ID: 8418809
TI Molecular cloning of a novel mRNA sequence expressed in cleavage stage mouse embryos.
AU Miyamoto H; Matsushiro A; Nozaki M
CS Department of Microbial Genetics, Osaka University, Japan.
SO Molecular reproduction and development, (1993 Jan) Vol. 34, No. 1, pp. 1-7.
Journal code: 8903333. ISSN: 1040-452X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
ED Entered STN: 26 Feb 1993
Last Updated on STN: 26 Feb 1993
Entered Medline: 5 Feb 1993
AB In an approach to study genes transcribed during early mouse development, a cDNA library was constructed from poly(A) RNA isolated from the 8-cell morula. The cDNA library was differentially screened with

labelled cDNA probes synthesized on poly(A) RNA isolated from the 8-cell morula or unfertilized eggs. Six clones which increased in abundance in the 8-cell morula were selected and further analyzed. Sequencing analyses showed that some of these clones corresponded to RNA transcripts from B1 and B2 repetitive sequences, as well as mRNA for cytochrome C oxidase I and NADH dehydrogenase III derived from the mitochondrial genome. One clone was not identical to any known sequences. The unidentified sequence (MO25) was found at low levels in the unfertilized egg, but increased at the 2-cell stage. The predicted amino acid sequence revealed that the MO25 gene may encode a Ca2+ binding protein.

=>